

WHAT IS CLAIMED IS:

1. A modified PAI-1 molecule in which two or more amino acid residues that do not contain a sulfhydryl group are each substituted by an amino residue that contains a sulfhydryl group wherein said modified PAI-1 molecule has an in vivo half-life that is
5 longer than the in vivo half-life of a wild-type PAI-1 protein.
2. The modified PAI-1 molecule of claim 1 which has an in vivo half-life of over 3 hours, 6 hours, 10 hours, 20 hours, 50 hours, 60 hours, 70 hours, 90 hours, 100 hours, 150 hours, 200 hours, 10 days, 12 days, 16 days, 30 days, or 60 days.
3. The modified PAI-1 molecule of claim 1 wherein said residue that contains a
10 sulfhydryl group is cysteine or methionine.
4. The modified PAI-1 molecule of claim 1 wherein said residue that contains a sulfhydryl group is cysteine.
5. The modified PAI-1 molecule of claim 1 wherein said two or more amino acid residues that do not contain a sulfhydryl group are selected from among positions 31,
15 97, 192, 197, 347, and 355 of the amino acid sequence of the PAI-1 protein of SEQ ID NO:2.
6. The modified PAI-1 molecule of claim 1 wherein said two or more amino acid residues that do not contain a sulfhydryl group are selected from one or more pairs of amino acid positions selected from the group consisting of 31 and 97, 192 and 347, and 197
20 and 355 of the amino acid sequence of the PAI-1 protein of SEQ ID NO:2.
7. The modified PAI-1 molecule of claim 1 that further comprises one or more amino acid substitutions that are not substitutions with a sulfhydryl-containing residue.
8. The modified PAI-1 molecule of claim 1 wherein said molecule inhibits urokinase plasminogen activator.
- 25 9. The modified PAI-1 molecule of claim 1 wherein said molecule inhibits tissue plasminogen activator.
10. The modified PAI-1 molecule of claim 1 wherein said molecule augments endogenous PAI-1 function.

11. A method of producing a modified PAI-1 molecule said method comprising:
(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule in which two or more amino acid residues that do not contain a sulfhydryl group are each substituted by an amino residue that contains a sulfhydryl group; (b) culturing the cell under
5 conditions suitable for expression of the modified PAI.

12. The method of claim 11 wherein said two or more amino acid residues that do not contain a sulfhydryl group are selected from among positions 31, 97, 192, 197, 347, and 355 of the amino acid sequence of the PAI-1 protein of SEQ ID NO:2.

10 13. The method of claim 11 wherein said two or more amino acid residues that do not contain a sulfhydryl group are selected from one or more pairs of amino acid positions selected from the group consisting of 31 and 97, 192 and 347, and 197 and 355 of the amino acid sequence of the PAI-1 protein of SEQ ID NO:2.

15 14. A method of treating or preventing a disease or disorder related to aberrant angiogenesis in a subject in need thereof, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

15. A method of treating or preventing cancer in a subject suffering therefrom, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

20 16. The method of claim 15 wherein said cancer is selected from the group consisting of breast cancer, colon cancer, ovarian cancer, lung cancer, prostate cancer, melanoma, leukemia, lung cancer, skin cancer, pancreatic cancer, bladder cancer, sarcoma, and uterine cancer.

25 17. A method of treating or preventing a cardiovascular disease or disorder in a subject, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

18. The method of claim 17 wherein said disorder is hyperfibrinolysis, hemophilia, or vessel leakage syndrome.

19. A method of treating or preventing a disease or disorder that is mediated by uPA, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

5 20. A method of treating or preventing a disease or disorder that is mediated by tPA, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

21. A method of treating or preventing uPA-mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

10 22. A method of treating or preventing tPA mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment or prevention is desired an effective amount of the modified PAI-1 molecule of claim 1.

23. A pharmaceutical composition comprising a therapeutically effective amount of the modified PAI-1 molecule of claim 1; and a pharmaceutically acceptable carrier.